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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,020	12/12/2003	Robert A. Casero	07410002AA	8827

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EXAMINER

SAIDHA, TEKCHAND

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 11/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/733,020	Applicant(s) CASERO ET AL.	
	Examiner Tekchand Saidha	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 September 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 1-21 and 27-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/12/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. ***Election***

Applicant's election without traverse of Group V (claims 22-26) and the sequences of SEQ ID NO: 1 and SEQ ID NO: 2 in the reply filed on 13 September 2006 is acknowledged.

2. **Claims withdrawn** :

Claims 1-21 & 27-35 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

3. ***Priority***

Applicant's claim for domestic priority under 35 U.S.C. 119(e), filed 13 June 2001, is acknowledged.

4. ***Drawings***

The drawings filed 12/12/2003 is acknowledged and is acceptable for examination purpose.

5. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

6. Claims 22-26 with respect to the sequences of SEQ ID NO: 1 and SEQ ID NO: 2 are under consideration in this Office Action.

7. ***Claim Rejections - 35 USC § 112*** (first paragraph)

Written Description

Claims 22-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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Claims 22-26 are drawn to a diagnostic or prognostic method for evaluating a response of a tumor to an antitumor polyamine analog, comprising the steps of: detecting expression of PAOh1/SMO Oxidase or a splice variant thereof in said tumor, wherein detection of said expression indicates that said tumor is responding or will respond favorably to treatment with said antitumor polyamine analog. The claims are directed to a genus of diagnostic or prognostic methods involving expression of any PAOh1/SMO Oxidase or a splice variant thereof, any type of tumor and using any antitumor polyamine analog, and wherein the detection is by using an antibody or PCR amplification to detect mRNA encoding PAOh1/SMO Oxidase or a splice variant thereof, with no defined structure of the nucleic acid, type of tumor or cell line or the name or chemical structure of the antitumor polyamine analog involved.

The specification provides guidance to a diagnostic or prognostic method for detecting expression of PAOh1/SMO Oxidase (SEQ ID NO: 1) and three additional splice variants, viz., PAOh2, PAOh3 & PAOh3 in selected lung cancer cell lines, wherein an increase in of PAOh1/SMO mRNA with increasing exposure time to polyamine analogs BENSpm, CPENSpm or MDL 72,527 is indicative that said cell line is responding favorably to treatment with said antitumor polyamine analog.

The specification does not contain any disclosure or description of the structure and function of all DNA sequences, nature of all the antitumor polyamine analogs or any type of the tumor associated with the claimed method. The genus of DNAs that comprise these above DNA, analogs or tumor or cell type is a large variable genus with the potentiality of includes a large number of variant species, analogs and many types of tumor or

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cell lines. Therefore, many structurally and functionally unrelated embodiments are encompassed within the scope of these claims. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

8. ***Enablement Rejection***

Claims 22-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a diagnostic or prognostic method for detecting expression of PAOh1/SMO Oxidase (SEQ ID NO: 1) in selected lung cancer cell lines, wherein an increase in of PAOh1/SMO mRNA with increasing exposure time to polyamine analogs BENSpm, CPENSpm or MDL 72,527 is indicative that said cell line is responding favorably to treatment with said antitumor polyamine analog and wherein the detection of PAOh1/SMO mRNA is carried out using PCR amplification, does not reasonably provide enablement for any diagnostic or prognostic method for evaluating a response of a tumor to an antitumor polyamine analog, comprising the steps of: detecting expression of PAOh1/SMO Oxidase or a splice variant thereof in said tumor, wherein detection of said expression indicates that said tumor is responding or will respond favorably to treatment with said antitumor polyamine analog.

The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of variant species, analogs and many types of tumor or cell lines broadly encompassed by the claims.

This is because of the nature of the method, the specificity of the lung cancer cell lines to the expression of PAOh1/SMO Oxidase as well as the nature of the antitumor polyamine analog (see example 5, page 19 of the instant

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specification). The claims are drawn to a diagnostic or prognostic method for evaluating a response of a tumor to any antitumor polyamine analog. In order for such a method to be effective specific method steps involving specific sequence(s), specific antitumor compound(s) and a specific cell line(s) are crucial.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature of the encoding DNA (or polynucleotide) encoding a specific PAOh1/SMO Oxidase or a splice variant having the desired enzymatic characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

9. **Claim Rejections - 35 USC § 112** (second paragraph)

Claims 22-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22, lines 4-5, recite the phrase 'will respond favorably to treatment'. The claim is indefinite because it is not clear what 'favorably' means, and may have an implied meaning of a cure. Deleting the word 'favorably' is suggested to overcome this rejection. Claims 23-26 are included in the rejection for failing to correct the defect present in the base claim(s).

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10. Claim 25, recite a step of detection, wherein antibody is used for detection of PAOh1/SMO Oxidase (enzyme). The claim is indefinite because claim 25 depends upon the elected method of claim 22, which the method involves detection of expression, which is detection of mRNA using PCR amplification, not an antibody to a protein. Cancellation of claim 25 is suggested because detection of expression of PAOh1/SMO Oxidase and detection of PAOh1/SMO Oxidase activity are separate methods.

11. Claims 22-24 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: In claim 22, addition of the detection step and a control step are required to complete the method step. Perhaps the limitation of claim 26, may be included in claim 22 to complete the detection step. Further, the method steps lack a control to compare. What is it compared with? Does it mean that a lack of detection of the enzyme is indicative that the tumor is not responding to treatment with antitumor polyamine analog. Clarification and addition of a control step is required to complete the method steps.

12. Prior art work of Lal et al. [WO200144448-A2, 21-Jun-2001; Priority 16-December-1999] teach an human oxido-reductase protein sequence which is 99.7% identical to Applicants' SEQ ID NO: 2. see the enclosed sequence search alignment between Lal's sequence and SEQ ID NO: 2]. This reference (sequence alignment only) is cited out of interest but has not been used in any art rejection.

13 No claim is allowed.

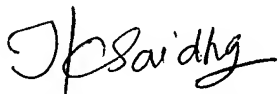
14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand

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Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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